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BARNES & THORNBURG
11 SOUTH MERIDIAN STREET
INDIANAPOLIS, IN 46204

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PCT

BARNES & THORNBURG

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Date of mailing
(day/month/year)

15 FEB 2005

Applicant's or agent's file reference

3220-75141

FOR FURTHER ACTION

See paragraph 2 below

International application No.

International filing date (day/month/year)

Priority date (day/month/year)

PCT/US04/14581

11 May 2004 (11.05.2004)

12 May 2003 (12.05.2003)

International Patent Classification (IPC) or both national classification and IPC

IPC(7): A61K 31/473, 31/4745 ; C07D 471/12, 491/02, 221/18 and US Cl.: 514/284, 283, 280, 279 ; 546/61, 51, 48, 41

Applicant

PURDUE RESEARCH FOUNDATION

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US

Mail Stop PCT, Attn: ISA/US
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Facsimile No. (703) 305-3230

Authorized officer

C.S. Aulakh

Telephone No. (571) 272-1600

Form PCT/ISA/237 (cover sheet) (January 2004)

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US04/14581

Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☐ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ in written format

☐ in computer readable form

c. time of filing/furnishing

☐ contained in international application as filed.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US04/14581

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees the applicant has:
- ☒ paid additional fees
 - ☐ paid additional fees under protest
 - ☐ not paid additional fees
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is
- ☐ complied with
 - ☒ not complied with for the following reasons:
See the lack of unity section of the International Search Report (Form PCT/ISA/210)

4. Consequently, this opinion has been established in respect of the following parts of the international application:
- ☒ all parts.
 - ☐ the parts relating to claims Nos. _____

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US04/14581

Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims <u>2-4, 7-11, 13, 14, 17, 18, 20, 23</u>	YES
	Claims <u>1, 5, 6, 12, 15, 16, 19, 21, 22, 24, 25</u>	NO
Inventive step (IS)	Claims <u>2-4, 7-11, 13, 14, 17, 18, 20, 23</u>	YES
	Claims <u>1, 5, 6, 12, 15, 16, 19, 21, 22, 24, 25</u>	NO
Industrial applicability (IA)	Claims <u>1-25</u>	YES
	Claims <u>NONE</u>	NO

2. Citations and explanations:

Claims 1, 5, 6, 12, 24 and 25 lack novelty under PCT Article 33(2) as being anticipated by Cho et al. (Chem Parm. Bull.).

Cho discloses isoquinoline derivatives having antitumor activity. The compound no. 13 (see page 901) disclosed by Cho is detrimental to the novelty of instant claims when R1 represents alkyl group, Q is O and Y represents methyl group in the instant compounds of formula of claim 1.

Claims 1, 5, 6 and 12 lack novelty under PCT Article 33(2) as being anticipated by Dyke et al. (Tetrahedron).

Dyke discloses isoquinoline derivatives. The compound no. 23 (see page 463) disclosed by Dyke is detrimental to the novelty of instant claims when R1 represents alkyl group, Q is O and Y represents methyl group in the instant compounds of formula of claim 1.

Claims 15, 16, 24 and 25 lack novelty under PCT Article 33(2) as being anticipated by Shamma et al. (Tetrahedron).

Shamma discloses synthetic approaches to camptothecin. The compounds III and IV (see page 2275) disclosed by Shamma are detrimental to the novelty of instant claims when Q is O and R1 represents H or OH in the instant compounds of formula of claim 15.

Claims 15, 16, 19, 21, 22, 24 and 25 lack novelty under PCT Article 33(2) as being anticipated by Shiyou (WO 01/30753).

Shiyou discloses camptothecin analogs. The compound no. 9 (see figure 1) disclosed by Shiyou is detrimental to the novelty of instant claims when Rc represents -CH2OH in the instant compounds of formula of claim 15.

Claims 2-4, 7-11, 13, 14, 17, 18, 20 and 23 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest the instant compounds.

Claims 1-25 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.

UNITED STATES RECEIVING OFFICE (RO/US) FEE COUPON AND RECORDING SHEET

☐ ADDITIONAL SHEET

IDENTIFICATION OF THE INTERNATIONAL APPLICATION

INTERNATIONAL APPLICATION NUMBER

PCT/US04/14581

INTERNATIONAL FILING DATE

11 May 2004 (11. 05. 2004)

APPLICANT (Name)

PURDUE RESEARCH FOUNDATION

PAYMENTS

REFUNDS

Payment on Filing				Deposit Account	Deposit Account	To Deposit Account	To Deposit Account
Deposit Account				DATE:	DATE:	DATE:	DATE:
<input type="checkbox"/> CASH/CHECK				<input type="checkbox"/> CASH/CHECK	<input type="checkbox"/> CASH/CHECK	<input type="checkbox"/> BY CHECK	<input type="checkbox"/> BY CHECK
160				1604	\$1,000.00		
151							
153							
800							
801							
802							
892							
Total Paid:				Total Paid:		Total Refunded:	
				\$1,000.00			
States included for 892:				892:			
States included for 893:				893:			

Date Mailed:

RO/US Authorization

SP

RO/US Authorization

RO/US Authorization

RO/US Authorization

RO/US Authorization

PCT RO/102(b) (U.S. VERSION)
(Rev. 10-82)

U.S. DEPARTMENT OF COMMERCE - Patent & Trademark

CHAPTER I
PCT TELEPHONE MEMORANDUM
FOR
LACK OF UNITY OF INVENTION



PCT No.: PCT/US04/14581

Examiner: Charanjit S. Aulakh

Attorney spoken to: Richard D. Conrad

Date of call: 16 November 2004

- ☒ Amount of payment approved: \$1,000.00
- ☒ Deposit account number to be charged: 10-0435
- ☒ Attorney elected to pay for ALL additional inventions
- ☐ Attorney elected to pay only for the additional inventions covered by
 - ☐ Group(s):
 - encompassing --
 - ☐ Claim(s):
- ☐ Attorney elected NOT to pay for any additional inventions, therefore, only the first claimed invention (Group I) covered by Claim(s) _____ has been searched.
- ☒ Attorney was orally advised that there is no right to protest for any group not paid for.
- ☒ Attorney was orally advised that any protest must be filed no later than 15 days from the mailing of the Search Report (PCT/ISA/210).

Time Limit For Filing A Protest

Applicant is hereby given 15 days from the mailing date of this Search Report in which to file a protest of the holding of lack of unity of invention. In accordance with PCT Rule 40.2, applicant may protest the holding of lack of unity only with respect to the group(s) paid for.

Detailed Reasons For Holding Lack of Unity of Invention:
Please See Continuation Sheet

Note: A copy of this form must be attached to the Search Report.

ATTACHMENT TO CHAPTER I PCT TELEPHONE MEMORANDUM FOR LACK OF UNITY OF INVENTION

Continuation of Detailed Reasons For Holding Lack of Unity of Invention:

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In order for more than one species to be examined, the appropriate additional examination fees must be paid. The species are as follows:

I. Compounds of formula of claim 1, pharmaceutical compositions containing these compounds and a method of using these compounds.

II. Compounds of formula of claim 15, pharmaceutical compositions containing these compounds and a method of using these compounds.

The claims are deemed to correspond to the species listed above in the following manner:

Species I : Claims 1-14

Species II : Claims 15-23

The following claim(s) are generic: Claims 24 and 25.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons:

There is no common core which in the Markush Practice, is a significant structural element shared by all of the alternatives; see PCT Administrative Instructions Annex B Part I (f) (i) (B) (1).

Note: A copy of this form must be attached to the Search Report.